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09/600,991	09/15/2000	Enzo Medico	471-162P	5174

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BIRCH STEWART KOLASCH & BIRCH  
PO BOX 747  
FALLS CHURCH, VA 22040-0747

EXAMINER

WEGERT, SANDRA L

ART UNIT PAPER NUMBER

1647

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/600,991

Applicant(s)

MEDICO ET AL.

Examiner

Sandra Wegert

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 November 2001.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 4-9, 11, 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 10 and 13 is/are rejected.
- 7) ☒ Claim(s) 1 and 2 is/are objected to.
- 8) ☒ Claim(s) 1-13 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 September 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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**DETAILED ACTION**

***Status of Application, Amendments, and/or Claims***

The Information Disclosure Statement received 15 September 2000 (Paper 6) has been entered into the record. Applicant's election with traverse of Invention I, (claims 1, 2, 3, 10 and 13) in Paper No. 11 is acknowledged. Claims 4-9, 11 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim.

The traversal is on the ground(s) that the polypeptides of Inventions I and II should be prosecuted in the same Inventive Group. Applicant's arguments are not persuasive, however since the Inventions were properly restricted as separate compositions having characteristic differences in structure and function. Although the polypeptides of Invention I and Invention II may have the same general tertiary structure, their being comprised of different growth factor subunits and their low relative homology (57-83%) precludes their being joined together as a single inventive Group, regardless of whether there is art on equivalent polypeptides. Furthermore, since a complete search of the art includes a search of the art that renders an invention obvious as well as anticipatory, the additional searches required for examination of Inventions I *with* Invention II would be extensive, thus presenting an undue burden for the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 2, 3, 10 and 13 are under examination in the Instant Application.

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**Informalities**

***Filing History***

The specification refers to PCT Application: PCT/EP99/00478 on page 1 of the specification. The current status of this file must be updated to include the Patent Number: WO 99/38967.

Appropriate correction is required.

***Abstract***

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. It should consist of one paragraph of 25 lines or less and 150 words or less.

Appropriate correction is required.

***Figures***

The drawings are objected to for reasons illustrated in Form PTO 948 (enclosed). Corrections will be required in the event there are allowable claims.

***Sequence Rules***

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules is

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not accompanied by the required reference to the relevant sequence identifier (i.e., SEQ ID NO:).

This occurs in claims 1, 2, 3, 10 and 13, for example.

### **Claim Rejections/Objections**

#### ***Claim Objections***

Claims 1 and 2 are objected to because they recite or encompass non-elected inventions.

Appropriate correction is required.

#### ***35 USC § 112, first paragraph - scope of enablement.***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

**The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Metron* peptide as defined in claim 3, for example, does not reasonably provide enablement for all variants of *Metron* as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are directed to a polypeptide of the formula:  $LS_{MSP}-HL_{MSP}-K1_{MSP}-K2_{MSP}-L-HL_{HGF}-K1_{HGF}-K2_{HGF}-D$ , an artificial peptide that probably resembles the  $\alpha$ -subunit of hepatocyte growth factor (HGF) or macrophage-stimulating protein (MSP) in its tertiary structure. The specification discloses *Metron* peptide as well as specific functions for the polypeptide. The scope of the patent protection sought by the Applicant as defined by the claims

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fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

The specification discloses an enabled utility for *Metron* polypeptide of the formula:  $LS_{MSP}-HL_{MSP}-K1_{MSP}-K2_{MSP}-L-HL_{HGF}-K1_{HGF}-K2_{HGF}-D$ , as to be used as a ligand of the *Met* receptor, for example. The specification is not enabling for sequences of the formula:  $(LS)_m-HL-K1-(K2)_n-(K3)_o-(K4)_p-B-HL-K1-(K2)_s-(K3)_t-(K4)_u-D$ , where  $m, n, o, p$  are 0 or 1. The specific activities of a representative number of proteins encompassed by this formula are not disclosed. Similarly, the specification is not enabling for sequences of the formula:  $(LS)_m-HL-K1-(K2)_n-(K3)_o-(K4)_p-B-HL-K1-(K2)_s-(K3)_t-(K4)_u-D$ , where  $n + o + p$  is an integer from 1 to 3 or 0. The specification is also not enabling for sequences of the formula:  $(LS)_m-HL-K1-(K2)_n-(K3)_o-(K4)_p-B-HL-K1-(K2)_s-(K3)_t-(K4)_u-D$ , where  $s, t, u$  are 0 or 1 and the sum of  $s, t$  and  $u$  is an integer from 1 to 3, or 0.

Claims 1 and 2 read on peptides in which, for example, entire kringle domains may be removed or substituted, presumably without changing *Metron's* function. However, the art contains numerous examples of peptide families whose members have even higher structural similarities than peptides of the Instant Application, yet disparate functions. The possible effect of changing even one amino acid in a polypeptide can be seen in Danilkovitch (1999, J. Biol. Chem., 274(42): 29937) in which certain single amino acid substitutions in various positions of Macrophage-stimulating protein (MSP) dramatically altered interactions with the *RON* tyrosine kinase receptor, while mutations of other residues had no effect. Similarly, Kopchick, et al (1994, US Patent 5,350,836) showed that small modifications at a single residue changed Bovine Growth Hormone from an agonist to an antagonist. These references and others demonstrate that

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it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to (a) the large quantity of experimentation required to determine how to use all variants of *Metron*, (b) the lack of direction or guidance in the specification regarding same - e.g., the lack of guidance regarding specific activity of all possible variations of *Metron* such as, for example, with *m*, *n*, *o*, or *p* equal to zero in the formula: (LS)<sub>m</sub>-HL-K1-(K2)<sub>n</sub>-(K3)<sub>o</sub>-(K4)<sub>p</sub>-B- HL-K1-(K2)<sub>s</sub>-(K3)<sub>t</sub>-(K4)<sub>u</sub>-D, (c) the lack of working examples to all variants of *Metron*, (d) the state of the art showing the unpredictability of function based on structural similarity of growth factor polypeptides, and (e) the breadth of the claims which embrace innumerable variants of *Metron*- undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

***Claim Rejections- 35 USC § 112, second paragraph - Indefiniteness.***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

**The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

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Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim refers to polypeptides which are identified by reference to Figures 1 and 2 of the specification. However, claimed subject matter should stand on its own without reference to a table or graph. One solution for identifying polypeptide sequences is to submit them in a sequence listing and label them by SEQ ID NO.

Claims 1, 2, 3, 10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 2, 3 and 10 are rendered indefinite because they are directed to recombinant proteins. It is unclear if the claims are directed to a compound containing the claimed polypeptide or a composition of several proteins. This rejection can be overcome by amending the claims to recite a *protein* (singular). Similarly, claim 13 recites pharmaceutical compositions containing recombinant proteins. This rejection can be overcome by amending the claim to recite a *composition*.

***Conclusion:***

Claims 1, 2, 3, 10 and 13 are rejected for the reasons listed above.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The



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examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

January 21, 2002

*Elizabeth C. Kemmerer*

ELIZABETH KEMMERER  
PRIMARY EXAMINER